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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/730,951	12/09/2003	Lee Dalton Jennings	AM100636	3667

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EXAMINER	
COPPINS, JANET L	
ART UNIT	**PAPER NUMBER**
1626	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/730,951	JENNINGS ET AL.	
	Examiner	Art Unit	
	Janet L. Coppins	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16 and 18-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-16,18 and 32-36* is/are allowed.

6)☒ Claim(s) *19-31 and 37-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-16 and 18-39 are currently pending in the instant application.

Response to Amendment

2. Receipt is acknowledged of Applicants' Amendment of December 13, 2006, which has been entered in the file. Accordingly, claim 17 has been cancelled, claims 1-4 and 16 as well as withdrawn claims 19 and 21-31 have been amended, and new claims 32-39 have been added.

3. Accordingly, claims 19-31 and 37-39, drawn to methods of use, are herein rejoined for examination, since the previously pending method of use claim, claim 17, has been cancelled.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 17 previously rejected under 35 U.S.C. 112, first paragraph, as not being fully enabled. The Examiner notes the cancellation of claim 17 and the amendatory changes to claim 19 with appreciation, in which Applicants have limited the scope to include specific diseases that are to be treated by administration of the claimed compound. However, claims 19-31 and 37-39 are newly rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, regarding the treatment of Alzheimer's disease and cancer.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,

4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case, the language of claim 19 encompasses many diseases and conditions that are not enabled in the specification, including Alzheimer's and cancer.

The nature of the invention

The nature of the invention is the treatment of certain disease conditions such as renal fibrosis, COPD, Alzheimer's disease, and cancer.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic or preventive regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to therapeutic and preventive effects of all diseases, whether or not the disease is affected by the inhibition of cellular levels of PAI-1 would make a difference.

It is the state of the art that there is no known cure or prevention for Alzheimer's disease, furthermore, there are only four medications available in the United States available to temporarily slow the early stages of Alzheimer's disease. The current drugs for the treatment of Alzheimer's disease, ARICEPT®, EXELON®, REMINYL® and COGNEX®, treat early stages of Alzheimer's disease by delaying the breakdown of acetylcholine. MEMANTINE®, which blocks excess amounts of glutamate, treats late stage Alzheimer's disease. (URL:http://www.cnn.com/2003/HEALTH/conditions/09/24/alzheimers.drug.ap/index.html).

Hence, in the absence of a showing of correlation between all the diseases claimed as capable of treatment by the inhibition of cellular levels of PAI-1 and since the treatment of Alzheimer's disease is mediated by the breakdown of acetylcholine or the inhibition of excess amounts of glutamate, one of skill in the art is unable to fully predict possible results from the administration of the compound of formula I due to the unpredictability of the disease.

Due to the unpredictable nature of cancer and the fact that over 3,000 different cancers exist, the various types of cancers have different causative agents, involve different cellular mechanisms, and differ in treatment protocol, thus no single compound exists presently that is known to treat *all* cancers as a blanket therapeutic. Furthermore, the Merck® manual currently has many cancer treating agents (over 12,000 compounds), yet they are only known to treat one cancer each.

The amount of direction or guidance present and the presence or absence of working examples

The Specification only describes a few *in vitro* assays of PAI-1 inhibition, demonstrating concentrations of the claimed compounds of Formula (1) needed to suppress 50%

suppression of cell proliferation (IC_{50} values), please see the Specification, pages 22-24. Given the scope of the many types of diseases/disorders included within the method claims, their varied etiologies, and the diversity of their patient populations, the disclosure in the Specification is insufficient to permit a person skilled in the art to practice a method for "inhibiting plasmogen activator inhibitor in a mammal" without naming any specific diseases of real-world relevance. While the Applicants cite specific diseases on pages 15-17 of the specification such as psoriasis, restenosis, and atherosclerosis, and cancers such as breast cancer and ovarian cancer and also provide many examples of how to prepare the instantly claimed compounds, there is no indication that the compounds can treat the entire scope of all named diseases. Applicants have provided evidence that the compounds are effective for treating murine colon tumors, however "the selection of the examples...used as the disclosure to support a claim must be adequately representative of the area covered by it," please see In re Cavallito et al. (CCPA 1970) 429 F2d 452, 166 USPQ 552. Therefore the specification is enabled for certain proliferative diseases including psoriasis, restenosis, and atherosclerosis, and certain cardiovascular diseases, however the instant specification is lacking significant data to accommodate as many diseases as the claims are alleging by reciting the broad mechanism of "inhibiting PAI-1." The test of enablement is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. " In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (citing In re Angstadt, 537 F.2d 489, 502-04, 190 USPQ 214, 217-19 (CCPA 1976)).

The breadth of the claims and the quantity of experimentation needed

The applicable rule is that "Each claim must be separately analyzed and given its broadest reasonable interpretation in light of and consistent with the written description." MPEP 2163(II)(1), citing In re Morris, 127 F.3d 1048, 1053-1054; 44 USPQ2d 1023, 1027 (Fed. Cir. 1997). Applying this rule to claim 19, the scope of diseases claimed to be prevented or treated would thereby include all diseases recited, including Alzheimer's, and all types and kinds of cancer, including such diverse types of cancer as sarcomas, epithelial tumors, breast cancer, ovarian cancer, leukemia, malignant lymphoma, prostate cancer, lung cancer, pancreatic cancer, renal cancer, etc. The quantity of experimentation needed is undue experimentation. Based on the unpredictable nature of the invention and the state of the prior art and the breadth of the claims, one of ordinary skill in the art would be burdened with undue "experimentation study" to determine whether the claimed compounds not only inhibit the activity of a chemokine, but have efficacy for treating Alzheimer's disease or cancer, both of which there is no known cure.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and whether Alzheimer's disease or any known cancer would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound of formula I for the treatment of Alzheimer's disease or cancer. As a result

necessitating one of skill to perform an exhaustive search for which diseases can be treated by the compounds of the instant claims in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search , but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factors and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test whether Alzheimer's disease can be treated by the compound encompassed in the instant claims, with no assurance of success.

One skilled in the art would require an undue quantity of experimentation to make or use the invention for inhibiting all of the claimed types of cancer; however, it would not require an undue quantity of experimentation for the skilled artisan to use the invention for treating or "inhibiting the growth of" certain types of cancer or cancerous tumors, **specifically** those mentioned in the disclosure, with a reasonable likelihood of success. The Examiner recommends limiting the scope of claims 19-31 and 37-39 to eliminate Alzheimer's disease and to encompass only certain very specific types of cancer for which Applicants can provide enabling support for.

Conclusion

6. In conclusion, claims 1-16 and 18-39 are pending in the application. Claims 19-31 and 37-39 are rejected. Claims 1-16, 18, and 32-36 appear allowable over the prior art.

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Coppins whose telephone number is 571.272.0680. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on 571.272.0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Janet L. Coppins
March 19, 2007

Joseph K. McKane
SPE, Art Unit 1626